UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,494	06/11/2001	Jeffrey Harris	27779/35932	3941

7590 08/27/2003

David W. Clough, P.h.D.
KATTEN MUCHIN ZAVIS ROSENMAN
Suite 1600
525 West Monroe Street
Chicago, IL 60661-3693

EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 08/27/2003

19

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,494	HARRIS ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2 and 6-58* is/are pending in the application.

4a) Of the above claim(s) *11 and 13-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-2, 6-10 and 12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-2, and 6-58 are pending.

1. Claims 11, and 13-58 stand withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

2. In view of the amendment filed 6/6/03, the following rejections remain.

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-2, and 6-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a composition comprising an effective amount of a β human chorionic gonadotropin fusion protein comprising the amino acid sequence of SEQ ID NO: 2 and a chitosan-based adjuvant, (2) a composition comprising an effective amount of a β human chorionic gonadotropin fusion protein consists of the sequence set forth in SEQ ID NO: 2 and a chitosan-based adjuvant for induction of infertility, **does not** reasonably provide enablement for (1) *any* composition consisting essentially of an effective of *any* fragment or *any* analog of β human chorionic gonadotropin protein fusion protein comprising SEQ ID NO: 2 and a chitosan-based adjuvant; (2) the said composition wherein the amount of *any* fragment or *any* analog of β human chorionic gonadotropin protein fusion protein comprising SEQ ID NO: 2 is about 25 μg; (3) the said composition wherein the chitosan-based adjuvant comprises an emulsion of chitosan, sodium hydroxide, any biodegradable oil, any surfactant, and any aqueous buffer; (4) the said composition wherein the chitosan-based adjuvant comprises an emulsion of chitosan, sodium hydroxide, any biodegradable oil, any surfactant, and any aqueous buffer and wherein the biodegradable oil is squalene; (5) the said composition wherein the chitosan-based adjuvant comprises an emulsion of chitosan, sodium hydroxide, any biodegradable oil, any surfactant, and any aqueous buffer; (6) the said composition wherein the chitosan-based adjuvant comprises an emulsion of chitosan, sodium hydroxide, any biodegradable oil, any surfactant, and any aqueous buffer and wherein the ratio of any βhCG proteins and/or fusions, fragments or analogs thereof to

adjuvant is in the range of about 1: 20 (w:w) to about 1:1500 (w/w), (7) the composition consisting essentially of an effective amount of an effective of *any* fragment or *any* analog of β human chorionic gonadotropin protein fusion protein comprising SEQ ID NO: 2 and a chitosan-based adjuvant wherein the adjuvant comprises chitosan, any metal salt, and an aqueous buffer, and (8) the composition consisting essentially of an effective amount of an effective of *any* fragment or *any* analog of β human chorionic gonadotropin protein fusion protein comprising SEQ ID NO: 2 and a chitosan-based adjuvant wherein the adjuvant comprises chitosan, any metal salt, and an aqueous buffer wherein metal salt is zinc acetate, nickel sulfate or copper sulfate for induction of infertility. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only two recombinant βhCG polypeptides comprising SEQ ID NO: 2 and 4. The specification further discloses that the recombinant polypeptide of SEQ ID NO: 2 is a fusion protein consisting of β human chorionic gonadotropin protein fused to a β-galactosidase (page 14) while the recombinant polypeptide of SEQ ID NO: 4 is a fusion protein consisting of β human chorionic gonadotropin protein fused to a FLAG peptide (page 15). The βhCG fusion proteins mentioned above are made recombinantly and they are useful for inducing infertility.

The specification does not teach how to make and use *any* composition mentioned above comprising *any* fragment and *any* analogs thereof of SEQ ID NO: 2 for inducing infertility because a fragment could be as little as one amino acid. There is insufficient guidance as to which fragment of SEQ ID NO: 2 is effective for stimulating antibody that binds specifically to the human chorionic gonadotropin, in turn, would be useful for inducing infertility. The specification defines the term "fragment" referring to a stretch of amino acid residues at least

about 5, 7, typically at least 9-13 amino acids or at least about 17 or more amino acids (page 9, line 20). Further, the term "analog" as defined in the specification o page 6 as any polypeptide differing from naturally occurring polypeptide by amino acid substitutions, deletions, and wherein the substitution may be non-conservative replacements, or conservative. There is insufficient guidance as to which amino acid within the fusion protein of SEQ ID NO: 2 that after substitution, deletion, insertion and/or modification will retain both structure and have similar function. Further, there is insufficient in vivo working demonstrating that any undisclosed compositions mentioned above are effective for inducing infertility or uses as a contraceptive.

Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure/function will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495).

Kuby *et al* teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide. Without the specific amino acid residues, it is unpredictable that immunizing any fusion protein will generate antibody that specifically binds to the βhCG, in turn, would be useful for inducing infertility.

Abaza *et al* teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody (the binding specificity of the antibody) against the site (See abstract, in particular). Given the indefinite number of undisclosed analog and fragment in a composition mentioned above, it is unpredictable which undisclosed composition comprising which undisclosed analog and fragment of SEQ ID NO: 2 would be useful as a composition for inducing infertility. Since the analog and fragment in the composition are not enabled, it follows that any composition comprising the analog or fragment of SEQ ID NO: 2 are not enabled. It also follows that the said composition wherein the amount of βhCG is about 25 μg is not enabled. It also follows that any composition consisting essentially of said analog or fragment of SEQ ID NO: 2 wherein the chitosan-based adjuvant comprises any emulsion of chitosan, sodium hydroxide, any biodegradable oil such as squalene,

any surfactant and any aqueous buffer, any metal salt such as zinc acetate, nickel sulfate, and copper sulfate, and aqueous buffer are not enabled.

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 6/6/03 have been fully considered but are not found persuasive.

Applicants' position is that claim 1 has been amended..

However, claim 1 still recites *any* composition consisting essentially of an effective of *any* "fragment" or *any* "analog" of β human chorionic gonadotropin protein fusion protein comprising SEQ ID NO: 2 and a chitosan-based adjuvant. Further, claim 8 still recites the ratio of any βCG proteins and/or any fusions, any fragments, or any analogs thereof. The specification does not teach how to make and use *any* composition mentioned above comprising *any* fragment and *any* analogs thereof of SEQ ID NO: 2 for inducing infertility because a fragment could be as little as one amino acid. There is insufficient guidance as to which fragment of SEQ ID NO: 2 is effective for stimulating antibody that binds specifically to the human chorionic gonadotropin, in turn, would be useful for inducing infertility. The specification defines the term "fragment" referring to a stretch of amino acid residues at least about 5, 7, typically at least 9-13 amino acids or at least about 17 or more amino acids (page 9, line 20). Further, the term "analog" as defined in the specification o page 6 as any polypeptide differing from naturally occurring polypeptide by amino acid substitutions, deletions, and wherein the substitution may be non-conservative replacements, or conservative. There is insufficient guidance as to which amino acid within the fusion protein of SEQ ID NO: 2 that after substitution, deletion, insertion and/or modification will retain both structure and have similar function. Further, there is insufficient in vivo working demonstrating that any undisclosed compositions mentioned above are effective for inducing infertility or uses as a contraceptive. Kuby *et al* teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization with a peptide fragment derived from a full-length polypeptide may result in

antibody specificity that differs from the antibody specificity directed against the native full-length polypeptide. Without the specific amino acid residues, it is unpredictable that immunizing any fusion protein will generate antibody that specifically binds to the βhCG, in turn, would be useful for inducing infertility.

Abaza *et al* teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody (the binding specificity of the antibody) against the site (See abstract, in particular). Given the indefinite number of undisclosed analog and fragment in a composition mentioned above, it is unpredictable which undisclosed composition comprising which undisclosed analog and fragment of SEQ ID NO: 2 would be useful as a composition for inducing infertility. Since the analog and fragment in the composition are not enabled, it follows that any composition comprising the analog or fragment of SEQ ID NO: 2 are not enabled. It also follows that the said composition wherein the amount of βhCG is about 25 μg is not enabled. It also follows that any composition consisting essentially of said analog or fragment of SEQ ID NO: 2 wherein the chitosan-based adjuvant comprises any emulsion of chitosan, sodium hydroxide, any biodegradable oil such as squalene, any surfactant and any aqueous buffer, any metal salt such as zinc acetate, nickel sulfate, and copper sulfate, and aqueous buffer are not enabled.

4. Claims 1-2, and 6-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* composition consisting essentially of an effective of *any* fragment or *any* analog of β human chorionic gonadotropin protein fusion protein comprising SEQ ID NO:.2 and a chitosan-based adjuvant; (2) the said composition wherein the amount of *any* fragment or *any* analog of β human chorionic gonadotropin protein fusion protein comprising SEQ ID NO: 2 is about 25 μg; (3) the said composition wherein the chitosan-based adjuvant comprises an emulsion of chitosan, sodium hydroxide, any biodegradable oil, any surfactant, and any aqueous buffer; (4) the said composition wherein the chitosan-based adjuvant comprises an emulsion of chitosan, sodium hydroxide, any biodegradable oil, any surfactant, and any aqueous buffer and wherein the biodegradable oil is squalene; (5) the said composition wherein the chitosan-based adjuvant

comprises an emulsion of chitosan, sodium hydroxide, any biodegradable oil, any surfactant, and any aqueous buffer; (6) the said composition wherein the chitosan-based adjuvant comprises an emulsion of chitosan, sodium hydroxide, any biodegradable oil, any surfactant, and any aqueous buffer and wherein the ratio of any βhCG proteins and/or fusions, fragments or analogs thereof to adjuvant is in the range of about 1: 20 (w:w) to about 1:1500 (w/w), (7) the composition consisting essentially of an effective amount of an effective of *any* fragment or *any* analog of β human chorionic gonadotropin protein fusion protein comprising SEQ ID NO: 2 and a chitosan-based adjuvant wherein the adjuvant comprises chitosan, any metal salt, and an aqueous buffer, and (8) the composition consisting essentially of an effective amount of an effective of *any* fragment or *any* analog of β human chorionic gonadotropin protein fusion protein comprising SEQ ID NO: 2 and a chitosan-based adjuvant wherein the adjuvant comprises chitosan, any metal salt, and an aqueous buffer wherein metal salt is zinc acetate, nickel sulfate or copper sulfate for induction of infertility.

The specification discloses only two recombinant βhCG polypeptides comprising SEQ ID NO: 2 and 4. The specification further discloses that the recombinant polypeptide of SEQ ID NO: 2 is a fusion protein consisting of β human chorionic gonadotropin protein fused to a β-galactosidase (page 14) while the recombinant polypeptide of SEQ ID NO: 4 is a fusion protein consisting of β human chorionic gonadotropin protein fused to a FLAG peptide (page 15). The βhCG fusion proteins mentioned above are made recombinantly and they are useful for inducing infertility.

With the exception of the specific fusion polypeptides of SEQ ID NO: 2 and 4, there is insufficient written description about the structure associated with function of *any* "analog" and *any* "fragment" of SEQ ID NO: 2 in the claimed composition for inducing infertility.

The specification discloses only two fusion proteins of SEQ ID NO: 2 and 4 comprising only human hCG joined to β-galactosidase protein or FLAG peptide. Given the lack of a written description of *any* additional representative species of "fragment" and "analog thereof" as encompassed by the claims, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 6/6/03 have been fully considered but are not found persuasive.

Applicants' position is that claim 1 has been amended.

However, claim 1 still recites *any* composition consisting essentially of an effective of *any* "fragment" or *any* "analog" of β human chorionic gonadotropin protein fusion protein comprising SEQ ID NO: 2 and a chitosan-based adjuvant. Further, claim 8 still recites the ratio of any βCG proteins and/or any fusions, any fragments, or any analogs thereof. Other than the specific fusion polypeptides of SEQ ID NO: 2 and 4, there is insufficient written description about the structure associated with function of *any* "analog" and *any* "fragment" of SEQ ID NO: 2 in the claimed composition for inducing infertility. Given the lack of a written description of *any* additional representative species of "fragment" and "analog thereof" as encompassed by the claims, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-2, and 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 91/16922 publication (Nov 1991, PTO 892) in view of EP 0368253 A2 (May 1990; PTO 1449) and Jones *et al* (The Lancet: 1295-1298; PTO 1449).

The WO 91/16922 publication teaches a composition (see page 25, lines 19-37, in particular) comprising various analog of β human chorionic gonadotropin (βhGC) fusion protein (chimera) such as hCG-beta/VSV-G fusion protein (full length beta subunit of human CG or fragment of hCG 39-56 (see page 13, line 7, in particular) fused to VSV-G or bovine LH (See page 10, line 6, Tables IV and XII, page 20, lines 7-13, page 23, line 10-18, in particular) in suitable vaccine adjuvant and suitable carriers, as known in the art (page 20, line 32-35, in particular). The reference β human chorionic gonadotropin (βhGC) fusion protein is a recombinant polypeptide (See pages 26, 42, Example 9, in particular).

The claimed invention in claim 1 differs from the reference only that the composition consisting essentially of a chitosan-based adjuvant.

The claimed invention in claim 2 differs from the teachings of the reference only that the composition wherein the amount of (βhGC) is about 25 μg.

The claimed invention in claim 7 differs from the teachings of the reference only that the biodegradable oil is squalene.

The claimed invention in claim 8 differs from the teachings of the reference only that composition wherein the ratio of βhGC fusion protein or analogs thereof to adjuvant is in the range of about 1:20 (w/w) to about 1: 500 (w/w).

The EP 0368253 A2 patent teaches chitosan-based adjuvant and a method of making said chitosan-based adjuvant for delivering any pharmaceutical such as human chorionic gonadotropin (See column 10, line 37, in particular) to a desired topical site of a test subject (See entire document, column 2, line 33-37, claims 1-10 of EP 0368253 A2, in particular). The EP 0368253 A2 patent teaches the chitosan-based adjuvant comprises an emulsion of chitosan, sodium hydroxide (See column 5, line 44-45, in particular), biodegradable oil such as eucalyptus oil, surfactant such as sodium lauryl sulfate or sorbitan and an aqueous buffer such as water (See column 11, line 10 bridging column 12, lines 1-30, in particular). The EP 0368253 A2 patent teaches the concentration of active ingredient to chitosan based delivery system can vary from as little as 0.0001 up to 5 percent or higher by weight of the chitosan-based adjuvant (column 11, liens 36-39, in particular) which is in the range of 1:20 (w/w) or 5% to about 1:500 (w/w) or 0.2%.

Jones *et al* teach a contraceptive vaccine composition comprising a human βhGC fragment such as hCG-β CT peptide 109-145 conjugate to a carrier protein such as diphtheria toxoid in synthetic adjuvant such as N-acetyl-glcosamine-3yl-acetyl-L-alanyl-D-isogluamine (CGP-11637), and saline-oil emulsion vehicle with oil phase consisting of the biodegradable oil squalene and surfactant such as mono-oleate as emulsifying agent (See page 1296, column 1, in particular). Jones *et al* teach the amount of βhGC ranges from 50 μg to 1000 μg (See Table 1, page 1296, in particular). Jones et al teach the formulation is safe and efficacious in laboratory animals' study and appears to be suitable for use in man (See page 1296, first paragraph, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the adjuvant as known in the art as taught by the WO 91/16922 publication for the chitosan-based adjuvant as taught by the EP 0368253 A2 using the vaccine formulation as taught by Jones et al for a composition comprising β human chorionic gonadotropin (βhGC) fusion protein or analog thereof and a chitosan-based adjuvant, wherein the amount of βhGC ranges from about 10 μg to 1500 μg as taught by The WO 91/16922 publication, the EP 0368253 A2 patent and Jones *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the EP 0368253 A2 patent teaches chitosan-based adjuvant is useful for delivering any pharmaceutical such as human chorionic gonadotropin (See column 10, line 37, in particular). Jones *et al* teach the amount of βhGC ranges from 50 μg to 1000 μg (See Table 1, page 1296, in particular) is safe and efficacious in laboratory animal study and appears to be suitable for use in man (See page 1296, first paragraph, in particular).

In re Kerkhoven, 205USPQ 1069 (CCPA 1980), recognized that "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose ... [T]he idea of combining them flows logically from their having being individually taught in the prior art" (see MPEP 2144.06). The term "about" in claim 8 expands the claimed range of the analog to the adjuvant to read on the reference range as taught by he EP 0368253 A2 patent (see column 11, liens 36-39, in particular), which is in the range of 1:20 (w/w) or 5% to about 1:500 (w/w) or 0.2%.

Applicants' arguments filed 6/6/03 have been fully considered but are not found persuasive.

Applicants' position is that claim 1 has been amended.

However, claim 1 still recites *any* composition consisting essentially of an effective of *any* "analog" of β human chorionic gonadotropin protein fusion protein comprising SEQ ID NO: 2 and a chitosan-based adjuvant. Further, claim 8 still recites the ratio of any βCG proteins and/or any fusions, any fragments, or any analogs thereof. The WO 91/16922 publication teaches a composition (see page 25, lines 19-37, in particular) comprising various analog of β human chorionic gonadotropin (βhGC) fusion protein (chimera) such as hCG-beta/VSV-G fusion protein (full length beta subunit of human CG or fragment of hCG 39-56 (see page 13, line 7, in particular) fused to VSV-G or bovine LH (See page 10, line 6, Tables IV and XII, page 20, lines 7-13, page 23, line 10-18, in particular) in suitable vaccine adjuvant and suitable carriers, as known in the art (page 20, line 32-35, in particular). The reference β human chorionic gonadotropin (βhGC) fusion protein is a recombinant polypeptide (See pages 26, 42, Example 9, in particular).

8. Claims 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 91/16922 publication (Nov 1991, PTO 892) in view of EP 0368253 A2 (May 1990; PTO 1449) and Jones *et al* (The Lancet : 1295-1298; PTO 1449) as applied to claims 1-2, and 6-8 mentioned above and further in view of US Pat No. 5,912,000 (June 1999, PTO 1449).

The combined teachings of the WO 91/16922 publication, the EP 0368253 A2 patent and Jones *et al* have been discussed supra.

The claimed invention in claim 9 differs from the teachings of the references only that the composition wherein the adjuvant comprises chitosan, a metal salt, and an aqueous buffer.

The claimed invention in claim 10 differs from the teachings of the references only that the metal salt is selected from the group consisting of zinc acetate, nickel sulfate, and copper sulfate.

The 5,912,000 patent teaches adjuvant such as chitosan for potentiating an immune response to any immunogen (See entire document, abstract, in particular). The reference chitosan comprises chitosan, a chelated metal ion such as copper, nickel or zinc from copper sulfate, nickel sulfate and zinc acetate (See column 4, Summary of Invention, lines 62-65, column 16, line 33-34, in particular) and an aqueous buffer such as PBS.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the chitosan based adjuvant as taught by the EP 0368253 A2 patent for the chitosan adjuvant comprising chitosan, a metal salt such as copper, nickel or zinc, and an aqueous buffer for a composition comprising β human chorionic gonadotropin (βhGC) fusion protein or analog thereof and a chitosan adjuvant comprising chitosan, a metal salt such as copper, nickel or zinc, and an aqueous buffer, wherein the amount of βhGC ranges from about 10 μg to 1500 μg as taught by The WO 91/16922 publication, the EP 0368253 A2 patent and Jones *et al.* From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the 5,912,000 patent teaches adjuvant such as chitosan for potentiating an immune response to any immunogen (See entire document, abstract, in particular).

Applicants' arguments filed 6/6/03 have been fully considered but are not found persuasive.

Applicants' position is that claim 1 has been amended.

However, claim 1 still recites *any* composition consisting essentially of an effective of *any* "analog" of β human chorionic gonadotropin protein fusion protein comprising SEQ ID NO: 2 and a chitosan-based adjuvant. Further, claim 8 still recites the ratio of any βCG proteins and/or any fusions, any fragments, or any analogs thereof.

9. The following new ground of objection and rejection are9* necessitated by the amendment filed 6/6/03.

10. Claims 6 and 9 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. The term "comprises" in claims 6 and 9 is open-ended. It expands the chitosan-based adjuvant in claim 6 or the adjuvant in claim 9 to include additional material in addition to the ones that are already recited in the claims. However, the composition in the base claim 1 recites a composition "consisting essentially of" which is narrower in scope than the dependent claims.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 1-2, 6-10 and 12 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

The "consisting essentially of" in Claim 1 represents a departure from the specification and the claims as originally filed. Applicant has not pointed out the support for said phrase. Further, it now changes the scope of the claimed composition.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

14. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of "βhCG **proteins and**/or fusions, fragments or analogs" in claim 8 has no antecedent basis in base claim 1. Base claim 1 recites a composition consisting essentially of an effective amount of a β human chorionic gonadotropin fusion protein comprising the amino acid sequence of SEQ ID NO: 2 or a fragment or analog thereof and a chitosan-based adjuvant.

15. Claim 12 is free of prior art.

16. No claim is allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

19. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
August 25, 2003

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600